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REMARKS CONCERNING CHASE'S RESULTS ON TESTING FOR ORDERED ALTER--ETC(U)

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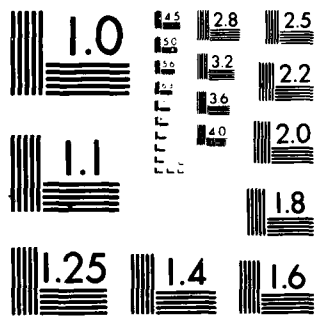
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REMARKS CONCERNING CHASE'S RESULTS ON TESTING FOR
ORDERED ALTERNATIVES⁽¹⁾

Tim Robertson

Department of Statistics
The University of Iowa
Iowa City, IA 52242

and F.T. Wright⁽²⁾

Department of Mathematics & Statistics
University of Missouri - Rolla
Rolla, MO 65401

Technical Report No. 79, 8

Department of Statistics and
Actuarial Science
The University of Iowa
Iowa City, Iowa 52242

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(1) This research was sponsored by the Office of Naval Research under ONR
contracts N00014-80-C0321 and N00014-80-C0322.

(2) This author is currently on leave at the National Science Foundation.

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REMARKS CONCERNING CHASE'S RESULTS ON TESTING FOR
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Tim Robertson and F. T. Wright

ABSTRACT

Chase (Biometrika (1974)) found a good approximation for the chi-bar-square ($\bar{\chi}^2$) and E-bar-square (\bar{E}^2) distributions for an important special case. These distributions are fundamental to the theory of order restricted tests. Chase had in mind the problem of comparing ordered dose levels with a control and considered the case where there are more observations on the control. He obtained a recursive relation for the limiting values of the coefficients in those distributions as the sample size on the control becomes infinite and the other sample sizes remain fixed and equal. His approximation is the result of an interpolation between critical values in this limiting case and critical values in the case where all the sample sizes are equal.

Starting with Chase's formula we derive a sharper recursion relation and table the limiting coefficients. This allows one to determine approximate P-values; to use critical values not included in Chase's tables and to apply these approximations to testing problems where other versions of the $\bar{\chi}^2$ and \bar{E}^2 distributions occur.

Key words and phrases: Order restricted inference, comparing ordered dose levels, Bartholomew's tests.

1. INTRODUCTION AND SUMMARY

The problem of testing the equality of several populations when these populations are known to satisfy an order restriction is discussed at length in Chapters 3 and 4 of Barlow, Bartholomew, Bremner and Brunk (1972). The chi-bar-square ($\bar{\chi}^2$) and E-bar-square (\bar{E}^2) distributions are fundamental to this theory. These distributions have tail probabilities which are linear combinations of chi-square and beta tail probabilities. The coefficients in these linear combinations are the probabilities that the order restricted, maximum likelihood estimates of normal means have a certain number of distinct values (called levels). These coefficients depend upon the precisions of the sample means as estimators of the corresponding population means. (Recall that the precision of the sample mean is the reciprocal of its variance (i.e., the quotient of the sample size and the population variance).) The computation of these coefficients has been the subject of a considerable amount of research. If the precisions are all equal and if the order restriction is simple then their values can be determined from the recursion formula given in Corollary B on page 145 of Barlow et al. (1972). This case, which is referred to as the equal weights case, is one of the few (even for simple orders) where computation of these coefficients is possible when the number of populations exceeds five. Thus, approximations are of interest.

Assume that we have $k+1$ normal means and that they are denoted by M_0, M_1, \dots, M_k . Consider the simple order restriction $M_0 \leq M_1 \leq \dots \leq M_k$ and let w_i denote the precision of the sample mean associated with M_i ; $i = 0, 1, 2, \dots, k$. We will henceforth refer to these precisions as

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weights. Chase (1974) found a good approximation for the case $w_1 = w_2 = \dots = w_k$ while $w_0/w_1 > 1$. He had in mind the problem of comparing the average responses, M_1, M_2, \dots, M_k , of several increasing dose levels with the average response, M_0 , to a zero dose control. As Chase noted, researchers often increase the sample size associated with the control over the sample sizes associated with the nonzero dose levels.

Chase obtained a recursion relation for the limiting values of the coefficients as the sample size on the control becomes infinite and the other sample sizes remain fixed and equal. His approximation is obtained by interpolating between this limiting value and the equal weights case. Starting with Chase's results we develop a generating function for these limiting coefficients which yields a more elegant recursion relation and using this relation we construct a table of these coefficients. This enables an investigator to obtain, by interpolation, approximate P-values for these tests and to use critical values not included in Chase's tables (his table is easy to use if the critical value of interest is included there). For a moderate number of populations, P-values can be computed using the table given here and for a larger number of populations a simple computer program can be written. The recursion formula given here is easy to program.

2. A GENERATING FUNCTION AND A RELATED RECURSION RELATION

We adopt Chase's notation. Suppose k dose levels are to be compared with a control. Index these treatments by the integers 0 to k , with 0 corresponding to the control and assume that dose level i is greater than

$i-1$ for $i=1,2,\dots,k$. We assume that the corresponding $k+1$ populations are normal with means and variances M_i and σ_i^2 and that we have independent random samples with sample sizes and means n_i and \bar{Z}_i ($i=0,1,\dots,k$). We are interested in testing $H_0: M_0 = M_1 = \dots = M_k$ against $H_1: H_0$ with $H_1: M_0 \leq M_1 \leq \dots \leq M_k$.

To illustrate the results we assume that the population variances are known, however the case of unknown variances is discussed in the next section. If Λ denotes the likelihood ratio, then

$$T = -2 \ln \Lambda = \sum_{i=0}^k w_i (\hat{\mu}_i - \bar{Z})^2 \quad (1)$$

where $w_i = n_i / \sigma_i^2$, $\bar{Z} = \sum_{i=0}^k w_i \bar{Z}_i / \sum_{i=0}^k w_i$ and $\hat{\mu} = (\hat{\mu}_0, \hat{\mu}_1, \dots, \hat{\mu}_k)$ gives the maximum likelihood estimates (MLE's) subject to the restrictions in H_1 . (Computation algorithms for $\hat{\mu}$ are discussed in detail in Barlow et al. (1972).) It is well known that, under H_0 ,

$$P[T \geq t] = \sum_{l=1}^{k+1} P(l, k+1; w) P[\chi_{l-1}^2 \geq t] \quad (2)$$

where χ_v^2 denotes a standard chi-square variable with v degrees of freedom ($\chi_0^2 \equiv 0$) and $P(l, k+1; w)$ denotes the probability, under H_0 , that the coordinates of $\hat{\mu}$ have exactly l distinct values. (The $P(l, k+1; w)$ are the coefficients discussed in the introduction.)

Because the $P(l, k+1; w)$ are computed under the assumption that H_0 holds, we may, in our study of them, assume that $M_0 = M_1 = \dots = M_k = 0$. In the equal weights case, $w_0 = w_1 = \dots = w_k$, we denote these probabilities by $P(l, k+1)$. It is well known (cf. Corollary A, page 143 of Barlow et al.

(1972)) that the generating function of the $P(l, k+1)$ is given by

$$\bar{E}_{k+1}(s) = \sum_{l=1}^{k+1} P(l, k+1) s^l = \binom{s+k}{k+1} \quad (3)$$

and that these probabilities satisfy the recursion relation

$$P(1, k+1) = kP(1, k)/(k+1) = (k+1)^{-1}, \quad P(k+1, k+1) = P(k, k)/(k+1) = [(k+1)!]^{-1} \quad (4)$$

and $P(l, k+1) = P(l-1, k)/(k+1) + kP(l, k)/(k+1)$

for $l=2, 3, \dots, k$ and $k=1, 2, \dots$.

These equal weights probabilities are given in Table A.5 of Barlow et al. (1972) for $k \leq 11$.

As was mentioned in the introduction, Chase studied the limiting value of $P(l, k+1; w)$ as $w_0 \rightarrow \infty$ and $w_1 = w_2 = \dots = w_k$ remain fixed. We denote these limiting values, which do not depend on the common value of w_1, w_2, \dots, w_k , by $Q(l, k+1)$ for $l=1, 2, \dots, k+1$. Chase proved the following recursion relation:

$$Q(l, k+1) = \sum_{m=0}^{k-l+1} Q(1, m+1) P(l-1, k-m)/2^{l-1}; \quad l=2, 3, \dots, k+1. \quad (5)$$

Of course, $Q(1, k+1)$ can be obtained from $\sum_{l=1}^{k+1} Q(l, k+1) = 1$. Starting with Chase's result, we obtain the generating function of the $Q(l, k+1)$.

Theorem. With the $Q(l, k+1)$ defined as above,

$$\bar{Q}_{k+1}(s) = \sum_{l=1}^{k+1} Q(l, k+1) s^l = s \binom{\frac{s-1}{2} + k}{k}. \quad (6)$$

Proof. The first step of the proof is to determine $Q(1, k+1)$ for $k = 0, 1, \dots$. Using (5), the fact that, for fixed k , $Q(l, k+1)$ is a probability distribution, and an interchange in the order of summation we have

$$\begin{aligned} Q(1, k+1) &= 1 - \sum_{m=0}^{k-1} Q(1, m+1) \sum_{l=2}^{k-m+1} P(l-1, k-m) 2^{-l+1} \\ &= 1 - \sum_{m=0}^{k-1} Q(1, m+1) E_{k-m}(1/2), \end{aligned}$$

which, applying (12.4) of Chapter 2 in Feller (1968), becomes

$$1 - \sum_{m=0}^{k-1} Q(1, m+1) (-1)^{k-m} \binom{-1/2}{k-m}.$$

Now consider the generating function of the sequence $\{Q(1, k+1)\}_{k=0}^{\infty}$;

$$\Psi(s) = \sum_{k=0}^{\infty} Q(1, k+1) s^k, \quad -1 < s < 1.$$

Using the above expression for $Q(1, k+1)$ and interchanging the order of summation, we see that

$$\begin{aligned} \Psi(s) &= (1-s)^{-1} - \sum_{m=0}^{\infty} Q(1, m+1) s^m \sum_{k=m+1}^{\infty} \binom{-1/2}{k-m} (-s)^{k-m} \\ &= (1-s)^{-1} - \Psi(s) [(1-s)^{-1/2} - 1] \end{aligned}$$

and so $\Psi(s) = (1-s)^{-1/2} = \sum_{k=0}^{\infty} \binom{-1/2}{k} (-s)^k$. Hence,

$$Q(1, k+1) = \binom{-1/2}{k} (-1)^k = \binom{k-1/2}{k}. \quad (7)$$

(Note that $Q(1, k+1) = E_k(1/2)$.)

Substituting (7) into (5) and using the resulting formula for $Q(l, k+1)$; $l=2, 3, \dots, k+1$, we write

$$\begin{aligned}
 \Theta_{k+1}(s) &= \binom{k-1/2}{k} s + s \sum_{l=2}^{k+1} \sum_{m=0}^{k-l+1} \binom{m-1/2}{m} P(l-1, k-m) (s/2)^{l-1} \\
 &= \binom{k-1/2}{k} s + s \sum_{m=0}^{k-1} \binom{m-1/2}{m} \sum_{l=2}^{k-m+1} P(l-1, k-m) (s/2)^{l-1} \\
 &= \binom{k-1/2}{k} s + s \sum_{m=0}^{k-1} \binom{m-1/2}{m} \binom{s/2 + k - m - 1}{k-m} \\
 &= s \sum_{m=0}^k \binom{m-1/2}{m} \binom{s/2 + k - m - 1}{k-m}.
 \end{aligned}$$

The identity (12.16) of Chapter 2 in Feller (1968), gives the desired expression for $\Theta_{k+1}(s)$.

There is a long-standing conjecture that the sum of the $P(l, k+1; w)$'s for odd l is equal to their sum for even l (cf. page 174 in Barlow et al. (1972)). If true, the result would be useful in computing the $P(l, k+1; w)$'s. This conjecture is equivalent to stating that the generating function of these coefficients vanishes at -1 . It is interesting to note that $\Theta_{k+1}(s)$ has a factor of $(s+1)$ so that $\Theta_{k+1}(-1) = 0$ for all k .

One could obtain the $Q(l, k+1)$ by expanding the polynomial $s^{\binom{s-1}{2} + k}$; however, a recursion formula like the one available for the $P(l, k+1)$ (cf. (4)) would be easier to implement.

Corollary. For $k=1, 2, \dots$,

$$\begin{aligned}
 Q(1, k+1) &= (2k-1)Q(1, k)/(2k), \quad Q(k+1, k+1) = Q(k, k)/(2k) \quad \text{and} \\
 Q(l, k+1) &= Q(l-1, k)/(2k) + (2k-1)Q(l, k)/(2k) \quad \text{for } l=2, 3, \dots, k.
 \end{aligned} \tag{8}$$

Proof. The desired results follow from the identity,

$$\begin{aligned}\Theta_{k+1}(s) &= \frac{(s/2 + k - 1/2)}{k} s \binom{s/2 + k - 3/2}{k-1} = \frac{s + 2k - 1}{2k} \Theta_k(s) \\ &= s(2k-1)Q(1,k)/(2k) + \sum_{l=2}^k s^l [Q(l-1,k)/(2k) + (2k-1)Q(l,k)/(2k)] \\ &\quad + s^{k+1} Q(k,k)/(2k).\end{aligned}$$

It is interesting to note that $Q(k+1,k+1) = (1/2)^k/k! = P(k,k)/2^k$ and that $Q(1,k+1) = (2k)!/(2^{2k}(k!)^2)$.

Using the results from the corollary, the $Q(l,k+1)$ were computed for $1 \leq k \leq 11$. Table 1 contains these values; for $k=8,9,10$ and 11 and $l > 8$, the $Q(l,k+1)$ are zero to five decimal places. So in the testing situation being considered one could compute P-values in the limiting case based on the $Q(l,k+1)$, in the equal weights case based on the $P(l,k+1)$ and interpolate on $w^{-1/2}$ where $w = w_0/w_1$. Chase found this interpolation scheme to be very satisfactory in computing critical values. To give some idea of its accuracy in computing P-values we considered $k=4$, a situation in which exact tail probabilities can be computed, $w=2,4$ and $t=6,9$. The exact values, with the approximations given by interpolation in parentheses, are as follows: for $w=2$, $P[T \geq 6] = .02915$ (.02893) and $P[T \geq 9] = .006704$ (.006770) and for $w=4$, $P[T \geq 6] = .02575$ (.02716) and $P[T \geq 9] = .006080$ (.006385). For moderate k we recommend computing the P-values given by (2) with the $P(l,k+1)$ from Table A.5 in Barlow et al. (1972) and with the $Q(l,k+1)$ from Table 1 and then interpolating on $w^{-1/2}$. For larger k one might wish to write a computer program to generate the $P(l,k+1)$ and $Q(l,k+1)$ recursively

from (4) and (8), to compute the appropriate tail probabilities and to do the interpolation.

3. OTHER APPLICATIONS

The distributional results discussed in the last section provide large sample approximations when exponential families are considered (cf. Theorem 4.5 of Robertson and Wegman (1978)). For example, one might wish to compare the ordered dose levels with a control by considering the proportions of individuals who exhibit a particular response to the various dosages. If p_i (p_0) is the proportion of individuals exhibiting this response when dose level i (the control) is administered, then one might wish to test $H_0^*: p_0 = p_1 = \dots = p_k$ vs. $H_1^* - H_0^*$ where $H_1^*: p_0 \leq p_1 \leq \dots \leq p_k$. Let \hat{p}_i , $i=0,1,\dots,k$, denote the corresponding sample proportions, which are assumed independent with \hat{p}_i based on a sample of size n_i , and let \bar{p}_i , $i=0,1,\dots,k$, denote the MLE's subject to the restrictions in H_1^* (cf. page 40 of Barlow et al. (1972)). Following the arguments used to prove Theorem 4.5 and Corollary 4.6 in Robertson and Wegman (1978), we see that with $\tilde{p} = \sum_{i=0}^k n_i \hat{p}_i / \sum_{i=0}^k n_i$, the LRT statistic, $-2\ln\Lambda$, is approximately equivalent to

$$T^* = [\tilde{p}(1-\tilde{p})]^{-1} \sum_{i=0}^k n_i (\bar{p}_i - \tilde{p})^2$$

as $n_i \rightarrow \infty$ with $n_i/n_0 \rightarrow w_i \in (0, \infty)$ for $i=0,1,\dots,k$. Furthermore, under the same assumptions on the sample sizes,

$$P[T^* \geq t] \rightarrow \sum_{\ell=1}^{k+1} P(\ell, k+1; w) P[\chi_{\ell-1}^2 \geq t]$$

with $P(\ell, k+1; w)$ defined as before. So T^* is a test statistic that can be used for large sample sizes and if $n_1 = n_2 = \dots = n_k$ and $n_0/n_1 = w \geq 1$, then Chase's results give approximate critical levels for certain α or the results presented here can be used to obtain approximate P-values.

Chase also considers testing homogeneity versus a trend in normal means when the variances are equal but unknown. The tail probabilities of the LRT statistic are linear combinations of beta tail probabilities and the coefficients are the same $P(\ell, k+1; w)$. Hence, the techniques discussed here apply in this situation too.

Robertson and Wegman (1978) and Robertson (1978) studied the problem of testing an order restriction as a null hypothesis. The tail probabilities of the null hypothesis distributions of the LRT statistics are again linear combinations of standard chi-square and beta probabilities. The coefficients are the probabilities that the order restricted maximum likelihood estimates of normal means have a specified number of levels. The results of Section 2 provide approximations for these testing problems for simple orders when one weight is larger than the others.

Robertson and Wright (1981) studied two problems where the LRT statistics have asymptotic null hypothesis distributions for which the results of Section 2 are possibly of use. Both of these problems involve tests concerning the relationship of the parameters of a multinomial population to a given set of possibilities for these parameters. One is a test of the equality of these two parameter sets when the alternative imposes a stochastic ordering between them and the other is a test of the null

hypothesis requiring the stochastic ordering. The appropriate null hypothesis, asymptotic distribution in each case involves the probabilities discussed in Section 2. The weights are the parameters of the given population so that the results here would be applicable if one of those parameters was relatively large while the others were (approximately) equal.

One might be interested in comparing increasing doses with more observations available on an intermediate dose level. Consider testing H_0 vs. H_1-H_0 (or H_0^* vs. $H_1^*-H_0^*$) with $w_j = w_0$ for $j \neq i$ and $w_i > w_0$. Assuming the variances are known, the LRT statistic and its tail probabilities are still given by (1) and (2), respectively. We need to find the limiting value of the $P(\ell, k+1; w)$ as $w_i \rightarrow \infty$, call them $Q_i(\ell, k+1)$, compute the P-values corresponding to the $P(\ell, k+1)$ and the $Q_i(\ell, k+1)$ and interpolate on $(w_i/w_0)^{-1/2}$. Recall that in computing the $P(\ell, k+1; w)$, we assume $M_0 = M_1 = \dots = M_k = 0$. Intuitively, as $w_i \rightarrow \infty$, $P(\ell, k+1; w)$ converges to the probability that the MLE, subject to H_1 and $\mu_i = 0$, has ℓ distinct values. The number of distinct values in the restricted MLE is the number of distinct values in the estimates of M_0, M_1, \dots, M_i plus the number of distinct values in the estimates of M_i, M_{i+1}, \dots, M_k minus one. Because these two numbers are independent and $Q_k(\ell, k+1) = Q(\ell, k+1)$,

$$Q_i(\ell, k+1) = \sum_{m=0}^{\ell-1} Q(m, i+1) Q(\ell-1-m, k-i+1). \quad (9)$$

Hence, the $Q_i(\ell, k+1)$ can be found from Table 1 and their generating function is

$$\Theta_{k,i}(s) = \sum_{l=1}^{k+1} Q_i(l, k+1) s^l = s^{\binom{s-1}{i} + i} \binom{\binom{s-1}{2} + k-i}{k-i}. \quad (10)$$

(Using the techniques in Chase's paper with those developed here, a rigorous proof could be constructed.) It is clear that similar remarks could be made for the case of unknown variances.

One might wish to compare increasing doses of two (or more) drugs against a common zero dose control. Suppose that there are $k_1(k_2)$ levels of drug 1(2) considered, that the control is again denoted by zero, that the dose levels on each drug are increasing, that the responses are normally distributed with means and variances M_0 and σ_0^2 and $M_{d,i}$ and $\sigma_{d,i}^2$ for $i=1,2,\dots,k_d$ and $d=1,2$ and that we have independent random samples with sample sizes and sample means n_0 and \bar{Z}_0 and $n_{d,i}$ and $\bar{Z}_{d,i}$ for $i=1,2,\dots,k_d$ and $d=1,2$. In testing $H_0^2: M_0 = M_{d,i}$ for $i=1,2,\dots,k_d$ and $d=1,2$ vs. $H_1^2-H_0^2$ with $H_1^2: M_0 \leq M_{1,1} \leq \dots \leq M_{1,k_1}$ and $M_0 \leq M_{2,1} \leq \dots \leq M_{2,k_2}$, the LRT statistic is

$$T_2 = w_0(\hat{\mu}_0 - \bar{Z})^2 + \sum_{d=1}^2 \sum_{i=1}^{k_d} w_{d,i}(\hat{\mu}_{d,i} - \bar{Z})^2$$

where the weights are, as before, the ratio of sample sizes to variances,

$$\bar{Z} = (w_0 \bar{Z}_0 + \sum_{d=1}^2 \sum_{i=1}^{k_d} w_{d,i} \bar{Z}_{d,i}) / (w_0 + \sum_{d=1}^2 \sum_{i=1}^{k_d} w_{d,i}) \text{ and}$$

$\hat{\mu} = (\hat{\mu}_0, \hat{\mu}_{1,1}, \dots, \hat{\mu}_{1,k_1}, \hat{\mu}_{2,1}, \dots, \hat{\mu}_{2,k_2})$ is the MLE subject to the restrictions in H_1^2 . The hypothesis H_1^2 imposes a partial order (not a total order as H_1 does) on the collection of means and a general computation algorithm for $\hat{\mu}$ in such cases is the minimum lower sets algorithm (cf. page 76 of Barlow et al. (1972)). Under H_0 , the tail probabilities of

T_2 are given by

$$P[T_2 \geq t] = \sum_{l=1}^{k_1+k_2+1} P(l, k_1+k_2+1; w) P[\chi_{l-1}^2 \geq t]$$

where $P(l, k_1+k_2+1; w)$ is the probability, under H_0 , of exactly l distinct values in $\hat{\mu}$. We can obtain the limit of $P(l, k_1+k_2+1; w)$ as $w_0 \rightarrow \infty$ and the other weights remain fixed and equal. As $w_0 \rightarrow \infty$, $P(l, k_1+k_2+1; w)$ converges to the probability that the MLE's, subject to the restrictions in H_1^2 with $M_0 = 0$, has l distinct values, but this is given by (9) with i replaced by k_1 and $k-i$ replaced by k_2 . If w_0 is significantly larger than the other weights (say 4 times as large) then this limiting distribution can be used for rough approximations. However, interpolation with the equal weights case is not possible because the equal weights probabilities are not known in this case. It would be of considerable interest to determine their values. As an approximation to the equal weights probabilities one could use (9) with $Q(\cdot, i)$ replaced by $P(\cdot, i)$ and then interpolate between the values of (2) based on the limiting values and these approximate values.

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Table 1. The $Q(l, k+1)$ for $1 \leq k \leq 11$.

k	l							
	1	2	3	4	5	6	7	8
1	.5	.5						
2	.375	.5	.125					
3	.3125	.47917	.1875	.02083				
4	.27344	.45833	.22396	.04167	.00260			
5	.24609	.43984	.24740	.05990	.00651	.00026		
6	.22559	.42370	.26343	.07552	.01096	.00078	.00002	
7	.20947	.40955	.27488	.08894	.01557	.00151	.00008	.00000
8	.19638	.39704	.28330	.10056	.02016	.00239	.00017	.00001
9	.18547	.38590	.28962	.11072	.02462	.00337	.00029	.00002
10	.17620	.37587	.29443	.11966	.02893	.00444	.00043	.00003
11	.16819	.36680	.29813	.12761	.03305	.00555	.00062	.00005

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1. REPORT NUMBER 8	2. GOVT ACCESSION NO. AD-A108144	3. RECIPIENT'S CATALOG NUMBER
4. TITLE (and Subtitle) Remarks on concerning Chase's results on testing for ordered alternatives.		5. TYPE OF REPORT & PERIOD COVERED Technical Report
		6. PERFORMING ORG. REPORT NUMBER
7. AUTHOR(s) Tim Robertson F.T. Wright		8. CONTRACT OR GRANT NUMBER(s) N00014-80-C-0321 N00014-80-C-0322
9. PERFORMING ORGANIZATION NAME AND ADDRESS Dept. of Statistics Dept. of Math University of Iowa University of Missouri Iowa City, Iowa 52242 Rolla, MO 65401		10. PROGRAM ELEMENT, PROJECT, TASK AREA & WORK UNIT NUMBERS
11. CONTROLLING OFFICE NAME AND ADDRESS Office of Naval Research Statistics and Probability Prog.-Code 436 Arlington, Virginia		12. REPORT DATE October 10, 1981
		13. NUMBER OF PAGES 14
14. MONITORING AGENCY NAME & ADDRESS (if different from Controlling Office)		15. SECURITY CLASS. (of this report) Unclassified
		15a. DECLASSIFICATION/DOWNGRADING SCHEDULE
16. DISTRIBUTION STATEMENT (of this Report) APPROVED FOR PUBLIC RELEASE: DISTRIBUTION UNLIMITED.		
17. DISTRIBUTION STATEMENT (of the abstract entered in Block 20, if different from Report)		
18. SUPPLEMENTARY NOTES		
19. KEY WORDS (Continue on reverse side if necessary and identify by block number) Order restricted inference, chi-bar-square distribution, E-bar-square distribution.		
20. ABSTRACT (Continue on reverse side if necessary and identify by block number) Chase (Biometrika (1974)) found a good approximation for the chi-bar-square ($\bar{\chi}^2$) and E-bar-square (\bar{E}^2) distributions for an important special case. These distributions are fundamental to the theory of order restricted tests. Chase had in mind the problem of comparing ordered dose		

levels with a control and considered the case where there are more observations on the control. He obtained a recursive relation for the limiting values of the coefficients in those distributions as the sample size on the control becomes infinite and the other sample sizes remain fixed and equal. His approximation is the result of an interpolation between critical values in this limiting case and critical values in the case where all the sample sizes are equal.

Starting with Chase's formula we derive a sharper recursion relation and table the limiting coefficients. This allows one to determine approximate P-values; to use critical values not included in Chase's tables and to apply these approximation to testing problems where other versions of the $\bar{\chi}^2$ and \bar{E}^2 distributions occur.

